Bandolier 122

Independent evidence-based health care

A bit of perspective

"..men are generally ready to believe what they want to believe" is a quote direct from Julius Caesar in his Gallic War. Most of us have our personal biases, honed by experiences bad and good. The trouble with biases is that they can obscure the truth, and we occasionally need to take a bit of a step back and question them.

Bandolier's first step back this month involved low dose aspirin. Prophylactic use of aspirin to prevent vascular events has been visited before, notably in ***Bandolier*** 86 and 108. The ***Bandolier*** Internet site has even given aspirin its own special place, where all the evidence we have found to date has been gathered together. Our view was that it was a good idea in many people, but that we had to beware of the harm that it also caused, especially in population terms. A new study from Scotland reinforces that bias.

When it comes to complementary therapies, ***Bandolier*** is sceptical. The perspective has often been one of promise, but the better the study, the more negative the result. The exception is with chemicals, like herbal remedies or glucosamine, where evidence is better. Avocado/soybean unsaponifiables (don't ask) seems to have some weight behind it, but noni juice is a no-no.

Bandolier also looks at perspectives relating to the loss of quality of life with osteoarthritis, and regaining quality back to the population norm on having a joint replacement. Lots of QALYs for our health economists to play with, and perspective. We could do with some clever folk to pull all the evidence on arthritis together to give even more perspective about what to do, when, and with whom.

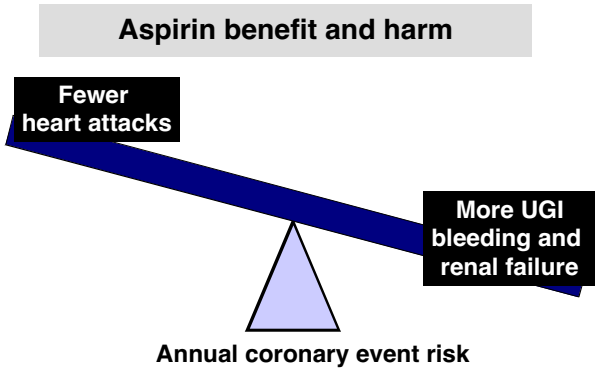
More evidence-based surgery

Not a request, but a rather a celebration. ***Bandolier*** often hears it said that surgery should be more evidence-based. Those who ask should stick their heads into a computer and do some searching. There is masses of good evidence on surgery out there - literally hundreds of good systematic reviews and lots of other good stuff.

A simple example of different methods of harvesting veins for use in coronary artery bypass surgery makes the point. There were lots of randomised trials, lots of patients, and consistent results. Super sensitivity analysis as well. Someone should be pulling this evidence together for professionals and public.

THE PRICE OF ASPIRIN

Were you to overhear conversations in any coal mining community, at some time you would come across a discussion about the price of coal. What you were listening to was no discussion about economics, but rather an oblique reference to the hidden costs of injuries and deaths resulting from coal extraction. In medicine the hidden costs are the costs of the adverse events that almost inevitably accompany attempts to generate benefit.



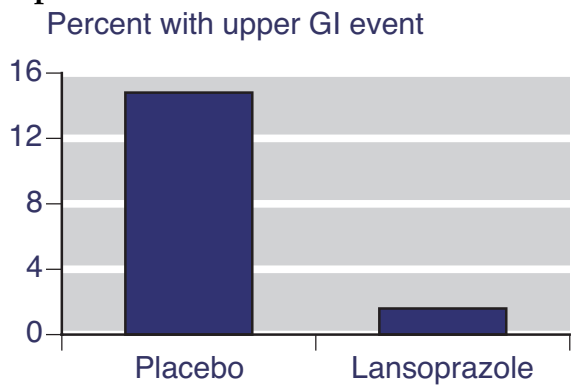
The balance of benefit and risk with aspirin prophylaxis was examined in ***Bandolier*** 86, where the main risk examined was upper gastrointestinal bleeding. There are other risks, though, mainly renal failure and congestive heart failure.

Preventing gastrointestinal events

Upper gastrointestinal bleeding can be reduced by concomitant use of proton pump inhibitors [1]. One hundred and twenty-three patients who had an ulcer complication after using low dose aspirin for more than one month, and who had Helicobacter pylori infection had their ulcers healed with triple therapy using PPI and antibiotics for one week followed by 20 mg famotidine twice a day for a further five

In this issue

Figure 1: Upper GI events with lansoprazole and placebo



weeks. Those patients whose Helicobacter infection had been cured were randomised to 100 mg aspirin and 30 mg lansoprazole or 100 mg aspirin and matching placebo, for 12 months, with follow up every two months. Patients were told to avoid taking NSAIDs. The primary end point was the recurrence of ulcer complications of bleeding, perforation or obstruction.

Results

Patients were 71 years old on average, and 70% were men. During the 12 months of the study, 14 upper gastrointestinal tract events were adjudicated by an end-points committee, and 10 were confirmed. One occurred in the 62 patients taking lansoprazole (2%) and nine in the 61 patients taking placebo (15%) (Figure 1). The relative risk was 0.1 (95% CI 0.01 to 0.8) and the number needed to treat with 30 mg lansoprazole for one year to prevent one upper gastrointestinal bleed was 8 (95% CI 4 to 27).

Low-dose aspirin costs

The costs of low dose aspirin have been explored in a massive study from Tayside [2]. In this population of about 400,000 people there is a well-established record-linking scheme, so that primary care prescriptions can be linked to medical history, other prescriptions, and hospital admissions and diagnostic interventions.

People who were dispensed one or more prescriptions for low dose aspirin (defined as not higher than 325 mg per day) at any time over the six years of 1990-1995 were included. For each subject there were 10 age and sex matched controls. Only new users were included.

The study outcomes were:

- hospital admission with a primary diagnosis of renal failure,
- creatinine of 150 µmol/L (the paper says 150 mmol/mL, which is a million times too high),
- hospital admission with a primary diagnosis of upper gastrointestinal event,
- endoscopy,
- histamine antagonist, proton pump inhibitor, or misoprostol prescription.

Results

Of the 17,244 subjects taking aspirin, 77% were aged 60 or older. There was an average of 2.53 years of observation per patient, during which aspirin was taken for 1.18 years. The implication was that compliance (concordance) was 47%.

Aspirin users had more renal and upper gastrointestinal adverse events (Table 1). The average annual cost was £18 per person for renal adverse events and £25 for gastrointestinal adverse events, compared with an average £2 for the aspirin and £5.50 for dispensing. These annual average costs were obtained by division of the total cost by the number of years of follow up, not by years of aspirin exposure.

A second analysis was limited only to low risk subjects free of disease at study entry (30% of total), and adjusted for

Table 1: Drug costs and costs of renal and upper gastrointestinal adverse events with low dose aspirin

	Over an average follow up of 2.5 years per patient			
	Aspirin users	Controls	Excess cost	Excess cost/year
Drug costs				
Aspirin	4.95		4.95	**1.96**
Dispensing cost	13.89		13.89	**5.49**
Total drug cost	18.84		18.84	**7.45**
Renal costs				
Renal admission	16.02	2.20	13.84	**5.47**
Dialysis	44.69	13.46	31.22	**12.34**
Total renal cost	60.71	15.66	45.06	**17.81**
Gastrointestinal costs				
GI admission	3.66	2.40	1.26	**0.50**
Endoscopy	44.19	18.99	25.19	**9.96**
Anti-ulcer drugs	46.72	10.95	35.80	**14.15**
Total GI cost	94.57	32.34	62.25	**24.60**
Total cost	174.12	48.00	126.15	**49.86**

Acutal exposure was 1.18 years of the average 2.53 years between the first prescription and end of the study

different risk factors between aspirin users and non-users. This produced a lower cost estimate of average annual cost of £2.90 per person for renal adverse events and £2.66 for gastrointestinal adverse events, and a total of £13 per patient per year.

Comment

This cost paper [2] is a brilliant read. It produces cogent arguments why the full analysis (called a pragmatic analysis in the paper) is likely to be the most sensible. It makes the point that it did not include costs involved with congestive heart failure, nor did it include any costs with any bleeding events not in the upper bowel. It also considers sources of bias, like use of non-prescribed aspirin or NSAIDs, and possible confounding by indication.

The projected annual costs, multiplied pro-rata for Scotland would be £3 to £11 million, and therefore for the UK would be ten times greater. And, of course, this is for newly treated patients, and with costs at 1996/7 prices.

It also examined costs per event prevented, using information from the largest meta-analysis (***Bandolier*** 108). Using the benefit of 16 events prevented per 1,000 people per year after a heart attack, the cost of one vascular event prevented would be £3,330. This used the pragmatic analysis and average costs over 2.5 years, not the 1.2 years of actual exposure, which would double the figure. At lower levels of cardiovascular risk the cost per event prevented rises substantially.

This paper is a must-read for those who provide guidance on prescribing in primary and secondary care. There is masses of good discussion that has to be read and understood, so that prescribing makes sense for individuals and for payers. It might also help to provide advice for the many older people who have several conditions with competing quality of life issues, to help decide what is best for them.

And aspirin resistance?

Just to confuse things further, there is now an acceptance that in some people aspirin may not prevent platelet aggregation. In those where this failure occurs, risks of vascular events are higher. It is too early to know just where this is leading, but for those who need to know more, a review [3] is a useful starting place.

References:
1 KC Lai et al. Lansoprazole for the prevention of recurrences of ulcer complications from long-term low-dose aspirin use. New England Journal of Medicine 2002 346: 2033-2038.
2 SV Morant et al. Cardiovascular prophylaxis with aspirin: costs of supply and management of upper gastrointestinal and renal toxicity. British Journal of Clinical Pharmacology 2003 57: 188-198.
3 R Altman et al. The antithrombotic profile of aspirin. Aspirin resistance, or simply failure? Thrombosis Journal 2004 2:1 (www.thrombosisjournal.com/contents/2/1/1).

AVOCADO/SOYBEAN UNSAPONIFIABLES FOR OA

Bandolier is occasionally taken to task over sins of omission. One reader commented that we paid insufficient attention to food additives for the treatment of osteoarthritis in a Cochrane review. The review [1] did indeed suggest that two trials of Avocado/soybean unsaponifiables (hereafter called ASU) suggested efficacy. A quick search found a third study, so a more detailed review seemed in order.

Background

ASU refers to extracts derived from one-third avocado oil and two-thirds soybean oil after hydrolysis. Chemical names and structures we do not have in detail, but this is presumably a fairly complex mix of chemicals. The main thing is that experiments show this mix to interfere with various cellular mediators, and prevent deterioration of synovial cells caused by interleukins, plus stimulating collagen synthesis in culture.

Search

The Cochrane review [1] had two trials [2,3], and a search of PubMed using free text terms avocado and arthritis produced two more [4,5].

Trials

All four trials (751 patients) were randomised and double blind, and compared ASU (predominantly 300 mg once a day) with placebo in people with osteoarthritis of knee or hip (Table 1). All used recommended standards for osteoarthritis trials, and all patients entered into the studies had osteoarthritis, pain of at least moderate intensity, and were using NSAIDs for pain control or had established pain of at least six months duration.

All four trials had similar outcomes, measuring pain, function, NSAID use and patient global outcome, and paid attention to adverse events and withdrawals. One [5] had a primary outcome of radiological joint space narrowing. Intention to treat and per-protocol analyses were both usually presented. Duration was three months in two, six to eight months in one, and 24 months in the fourth.

The design was an add-on to NSAID therapy, with an assumption that at least one month, and possible three, was needed for maximum effect of ASU. All the trials allowed for adjustment of NSAID dose according to requirement, either through withdrawal during the trial, or withdrawal at the start, followed by add-back as needed.

Results

Details of trials are given in Table 1. Three trials [2-4] had better pain and functional ability with ASU + NSAID compared with placebo + NSAID over three to six months. In all three, better pain relief was achieved with a lower dose of NSAID. Both these effects took some months to develop.

Table 1: Details of trials for ASU in OA

Reference	Design	Treatments	Outcomes	Results
Blotman et al. Revue du Rhumatisme 1997 64: 825-834 France [2]	Randomised, double-blind, placebo-controlled, add-on to NSAID therapy Patients aged 45-80 with OA hip or knee using ACR criteria, using NSAIDs (mean 80 mg diclofenac), and with pain 25/100 mm or more Quality score 4/5	ASU 300 mg per day or placebo Three months, with NSAID continued for first 45 days, with reduction according to need in second 45 days 164 patients recruited	Consumption of NSAID Pain score Global evaluation by patient Adverse events Discontinuations	Groups identical at baseline Using NSAIDs at end: 33/77 ASU, 53/76 placebo No difference in pain score Global good and very good at end: 46/76 ASU, 25/73 placebo Patients with AE second 45 days 1 ASU, 4 placebo AE withdrawals 1 each group
Maheu et al. Arthritis & Rheumatism 1998 41: 81-91 France [3]	Randomised, double-blind, placebo-controlled, add-on to NSAID therapy Patients aged 45-75 with OA hip or knee using ACR criteria, using NSAIDs ,and with pain 30/100 mm or more Quality score 4/5	ASU 300 mg per day or placebo Eight months, with NSAID withdrawn for 15 days before start, and then allowed as necessary 164 patients recruited	Lequesne index Pain score Functional ability NSAID use Analgesic use Global evaluation by patient Adverse events Discontinuations	Groups identical at baseline Significant improvement in Lequesne index, pain score (by mean 10/100 mm), functional ability Use of NSAID at end: 34/84 ASU, 44/78 placebo Global good and very good 53/84 ASU, 30/78 placebo Patients with AE 23/85 ASU, 20/79 placebo AE withdrawals 1/85 ASU, 3/79 placebo
Appelboom et al. Scand J Rheumatology 2001 30: 242-247 Belgium [4]	Randomised, double-blind, placebo-controlled, add-on to NSAID therapy Patients aged 45-80 with knee OA using ACR criteria, using NSAIDs (mean 135 mg diclofenac), and with pain 30/100 mm or more Quality score 3/5	ASU 300 mg per day, ASU 600 mg per day, or placebo Three months, with symptomatic use of NSAID or analgesic 260 patients recruited	NSAID use over days 30-90 Pain score Lequesne index Global evaluation by patient Adverse events Discontinuations	Groups identical at baseline NSAID use reduced significantly for ASU groups, with lower pain score and better Lequesne index More than 50% decrease in NSAID use by days 60-90: 46/86 ASU 300, 49/86 ASU 600, 24/88 placebo At least good score by patient at end: 58/86 ASU 300, 47/86 ASU 600, 25/88 placebo Patients with AE: 28/86, 24/86, 23/88
Lequesne et al. Arthritis & Rheumatism 2002 47: 50-58 France [5]	Randomised, double-blind, placebo-controlled, add-on to NSAID therapy Patients aged 50-80 with hip OA using ACR criteria, using NSAIDs (mean 55 mg diclofenac), with pain for 6 months or more, and joint space of at least 1 mm Quality score 4/5	ASU 300 mg per day or placebo 24 months, with symptomatic use of NSAID or analgesic 163 patients recruited	Joint space at 24 months NSAID use Pain score Lequesne index Global evaluation by patient Adverse events Discontinuations	Groups identical at baseline Joint space significantly less narrow in those with initial joint space less than 2.5 mm, but not more than 2.5 mm or total sample NSAID use declined from 55 mg diclofenac equivalent a day to 25 mg a day in both groups No difference in pain score (reduced from 50 mm to 31 mm) or Lequesne index Global slightly better or better: 31/85 ASU, 30/78 placebo Patients with AE: 39/85 ASU, 39/78 placebo AE withdrawals 2 each group

For example, Figure 1 shows pain reduction over three months and Figure 2 shows the concomitant average daily equivalent dose of diclofenac in one trial [3].

A fourth trial [5] showed no difference in pain, functional ability, or daily NSAID use over 24 months. This trial examined only patients with osteoarthritis of the hip, with a relatively low (50 mg diclofenac equivalent) initial daily use of NSAID. Joint space narrowed from an initial mean of 1.9 mm to 1.7 mm over two years in both groups, but with a significant reduction in narrowing in those patients whose initial joint space was below the median.

The number needed to treat (NNT) for one more patient to achieve at least a global outcome of good or better at the end of the trial with ASU + NSAID compared with placebo + NSAID was 3.6 (2.8 to 5.0; Table 2) in three trials [2-4]. All three trials had similar levels of efficacy (Figure 3). For one patient to be on no NSAID or to have an NSAID dose reduction of more than 50% was 4.3 (3.2 to 6.5). The one trial looking at dose showed no difference between 300 mg or 600 mg of ASU a day.

In all four trials there was no difference in the number of patients reporting at least one adverse event (Table 2). Adverse event withdrawals were low and the same in the three trials reporting it.

Figure 1: Pain scores with ASU and placebo

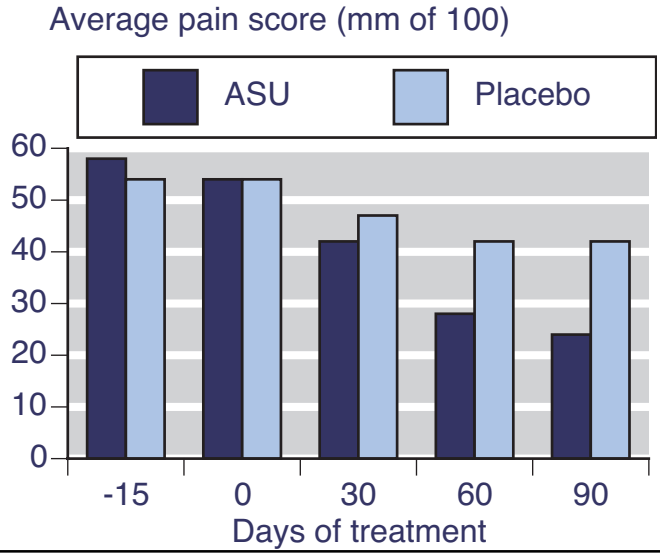


Table 2: NNTs for ASU compared with placebo when added to NSAID therapy in OA

Outcome	Trials	Number/total with		Relative benefit 95% CI	NNT 95% CI
		ASU + NSAID	Placebo + NSAID		
Not using NSAID or dose reduced by more than 50% at end of trial	3	189/333 (57%)	81/242 33%)	1.7 (1.4 to 2.1)	4.3 (3.2 to 6.5)
Patient global outcome at least good at end of trial	3	204/332 (61%)	80/239 (33%)	1.9 (1.5 to 2.3)	3.6 (2.8 to 5.0)
Patients reporting any adverse event during the trial	4	123/418 (29)	92/318 (29)	1.1 (0.8 to 1.5)	not calculated

Comment

This is interesting. We may be a bit hazy about what ASU are chemically, and be without an overabundance of literature on what they do, but there is some evidence from three well-designed and conducted trials that ASU achieves the double whammy of both reducing pain and reducing NSAID consumption. The fly in the ointment is that a longer study of osteoarthritis in the hip showed no difference at all in any outcome. The evidence we have is of good quality, the trials are valid, and we have a reasonable number of patients in the trials.

What are we to make of this? All four trials used ASU from one source (a company called Pharmascience in France), which probably sponsored three of the trials. So differences in the results do not come about because of different preparations. In the two trials looking at both knee and hip, similar benefit was found. The one looking at only knee osteoarthritis was positive, the one looking at only hip osteoarthritis was negative. It is something of a mystery. The only major difference is duration, and we must wait to see if other longer duration trials produce negative results.

Our NNTs come only from the three positive trials, because the negative trial did not report outcomes in a way we could use for NNT calculations. Given that NSAIDs are implicated with renal, cardiovascular, and gastrointestinal harm, reducing their use must be a good thing.

Figure 2: NSAID consumption with ASU and placebo

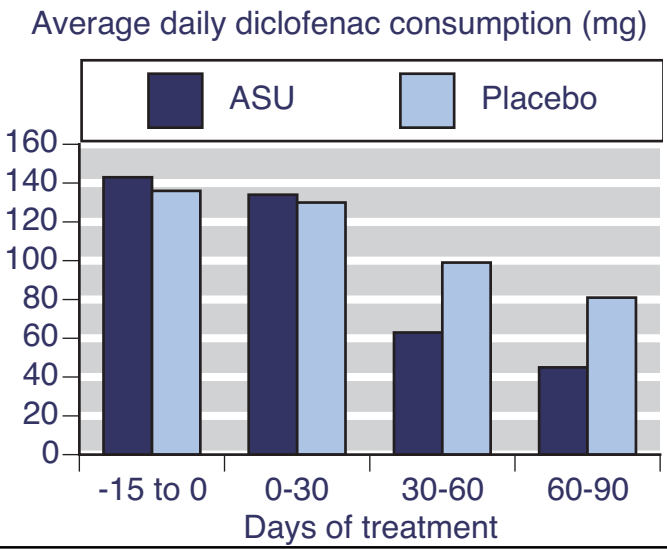
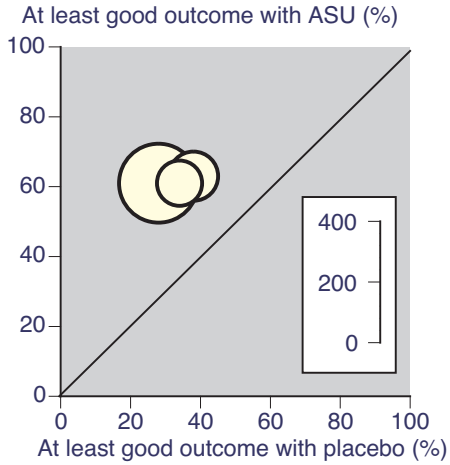


Figure 3: Global outcomes with ASU and placebo



So should people with osteoarthritis take ASU? On the evidence we have, it might make well make sense over the short term. The problems we have are with supply (where can we obtain it?), availability on prescription (depends on local rules), pharmaceutical consistency and quality (need for international quality and control), and perhaps above all a definition of what it is we might be taking. A definition of what is in ASU exists, with background science to support clinical observations [6], so there is some evidence that this is more than voodoo science.

References:

1 CV Little et al. Herbal therapy for treating osteoarthritis (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd.

2 F Blotman et al. Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. Revue du Rheumatologie [English edition] 1997 64: 825-834.

3 E Maheu et al. Symptomatic efficacy of avocado/soybean unsaponifiables in the treatment of osteoarthritis of the knee and hip. Arthritis & Rheumatism 1998 41: 81-91.

4 T Appelboom et al. Symptoms modifying effect of avocado/soybean unsaponifiables (ASU) in knee osteoarthritis. Scandinavian Journal of Rheumatology 2001 30: 242-247.

5 M Lequesne et al. Structural effect of avocado/soybean unsaponifiables on joint space loss in osteoarthritis of the hip. Arthritis & Rheumatism 2002 47: 50-58.

6 YE Henrotin et al. Avocado/soybean unsaponifiables increase aggrecan synthesis and reduce catabolic and proinflammatory mediator production by human osteoarthritic chondrocytes. Journal of Rheumatology 2003 30: 1825-1834.

How good is a joint replacement?

Patient perspectives of osteoarthritis are not always captured by clinical trials, which use outcomes like WOMAC scales, or pain in the rather contrived setting of walking on a flat surface. Though these are important outcomes, and necessary for proving clinical efficacy, they do not always help patient or professional understand the full benefit of a treatment. With surgery it may be more difficult to understand the benefits, especially when the aim is to cure as much as ameliorate symptoms.

Understanding the patient perspective, and the underlying problems with arthritis should come first. A UK survey of 3,127 patients whose diagnosis of osteoarthritis had been confirmed by a GP, contained results on 18 quality of life indicators [1]. Figure 1 shows that sleeping, walking, and such everyday activities as bathing and dressing affected people often. It is little wonder that in chronic diseases, the largest negative impact on quality of life is seen in musculoskeletal disorders of osteoarthritis, rheumatoid arthritis, and back pain (***Bandolier*** 83).

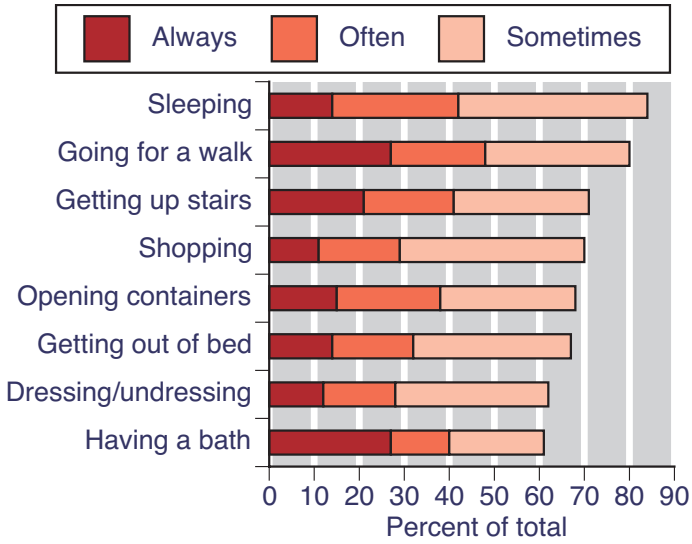
A North Yorkshire survey suggested that over and above those already having a joint replacement, about 380/100,000 persons aged 55 and over might benefit from hip replacement, with as few as 45/100,000 actually on a waiting list (***Bandolier*** 103). If quality of life is low with arthritis, what happens to quality of life after joint replacement?

Study

An Australian study [2] reported on part of an ongoing prospective trial that included patients of nine orthopaedic surgeons in four Sydney hospitals. Patients with a diagnosis of osteoarthritis or rheumatoid arthritis were eligible, though here only results for osteoarthritis were reported.

Preoperatively, and every three months after joint-replacement operation for 12 months, patients were mailed monthly self-administered WOMAC and SF-36 questionnaires, and reminded to complete them by telephone. WOMAC is the Western Ontario and McMaster Universities Osteoarthritis index, measuring dimensions of pain, stiffness and physical function. SF-36 is a generic quality of life questionnaire assessing 36 items in eight domains. WOMAC scoring is on a 1-5 scale, which was transformed to a 0-100 scale, and SF-36 scores on a 0-100 scale.

Figure 1: Everyday tasks causing problems for patients with OA



Results

There was a 67% response rate in 252 patients recruited. The 194 participants had an average age of 74 years, and 86 had osteoarthritis of the hip and 108 of the knee. The overall follow up averaged 11 months. Disease duration averaged 10 years, and half were women.

There were significant improvements for all three areas of the WOMAC scale of physical function (Figure 2), where lower scores are better), pain, and stiffness for both hip and knee replacement. For physical functioning (Figure 2), hip replacement resulted in a beneficial reduction in the WOMAC score from 37 to 12.

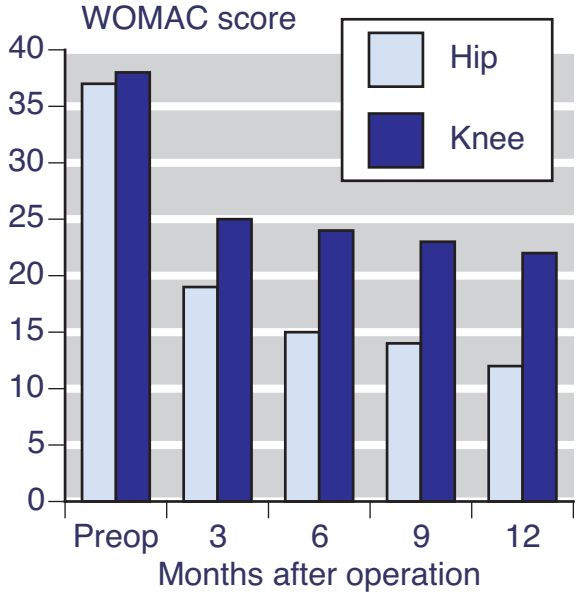
There were significant improvements in the SF-36 quality of life questionnaire for most of the eight domains for both hip and knee replacement (Table 1, where higher scores are better). Bodily pain, physical functioning and physical role

Table 1: Preoperative and 12 month scores in SF-36 domains (0-100) for hip and knee replacement

	Hip replacement		Knee replacement	
SF-36 domain	**Preop**	**12 months**	**Preop**	**12 months**
General health	66	**74**	71	70
Bodily pain	33	**73**	33	**57**
Physical function	27	**67**	25	**50**
Physical role function	15	**59**	18	**50**
Social function	53	**89**	59	**77**
Mental health	71	**82**	70	77
Emotional role function	60	72	54	65
Vitality	47	**68**	47	**59**

Bold, shaded areas show statistical significance at 5% level. Higher scores indicate a better health state.

Figure 2: Physical functioning (WOMAC). Higher scores are worse.



functioning were most improved. Exceptions were emotional role function for both hip and knee, and general health and mental health for knee replacements, though both scores were high initially.

For both of the scales the first three months following joint replacement found the largest changes. Improvements tended to continue over the succeeding nine months, but at a lower rate.

Comment

These are major beneficial changes from joint replacement surgery. A previous report [3] demonstrated that at all ages from 55 years, hip replacement brought SF-36 scores for osteoarthritis patients back to population norms for age. Knee replacement was almost as good, except that in the age group of 55-64 years population norms were not all achieved.

For most patients having hip or knee replacement large quality of life gains will occur. With the modest cost of the operations, this will mean the cost per quality-adjusted life year will be low. These results also underscore the quality of life losses by people with osteoarthritis who have not had a joint replacement. Large gains in quality of life after joint replacement means that quality of life must have been pretty low with osteoarthritis. This ties together the information we have rather neatly.

References:
1 B Crichton, M Green. GP and patient perspectives on treatment with non-steroidal anti-inflammatory drugs for the treatment of pain in osteoarthritis. Current Medical Research & Opinion 2002 18: 92-96.
2 CJ Bachmeier et al. A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. Osteoarthritis and Cartilage 2001 9: 137-146.
3 LM March et al. Outcomes after hip or knee replacement surgery for osteoarthritis. Medical Journal of Australia 1999 171: 235-238.

MYTHBUSTER – HIP REVISION

Bandolier has come across the suggestion that having a hip re-done is a bad thing, often given as an excuse for not doing hip replacements originally on younger people with arthritis. A systematic review [1] gives some answers.

Review and results

A MEDLINE search to the year 2000 sought English-language citations relating to hip revisions. Thirty-nine articles reporting on 40 cohorts and 2,578 patients were found. Functional outcome measures were sought as categorical outcomes (excellent, good etc), and Harris hip scores.

The mean age of patients was 67 years, 64% were women and osteoarthritis was the cause of the primary operation. Overall, 68% had an excellent or good outcome. Harris hip scores increased after the revision by an average of 37 points. The average re-revision rate was 6%, and mortality associated with the operation was 2.3%.

Comment

An interesting review, with a good analysis of adverse events. Revision of hip replacement seems to be a good buy.

Reference:
1 KJ Saleh et al. Functional outcome after revision hip arthroplasty. A metaanalysis. Clinical Orthopaedics and Related Research 2003 416: 254-264.

MYTHBUSTER – NONI JUICE

Noni juice comes from a Polynesian plant. ***Bandolier*** was sent literature, and readers asked if it worked.

The literature we received claimed an analysis of 15,000 patients treated with noni juice for conditions spanning the A-Z of clinical conditions, from allergy, though arthritis, asthma, cancer, HIV, obesity, to well being. The claims for benefit were usually in the 70%-90% range.

A brief search revealed a systematic review [1]. Neither this, nor any other searches found any reports in the medical literature of randomised trials, or any trials of any sort, for that matter. Diluted noni juice does funny things to cells in test tubes, but then so might diluted orange juice.

Comment

Noni juice has no respectable evidence to back up any claims. The one guarantee is that it relieves your pocket of money because it is very expensive. The unrequested literature ***Bandolier*** received suggested something of a get-rich-quick sales operation. Caveat emptor.

Reference:
1 M-Y Wang et al. Morinda citrifolia (Noni): a literature review and recent advances in Noni research. Acta Pharmacologica Sinica 2002 23: 1127-1141.

Vein harvesting techniques compared

Bandolier 119 was intrigued by a paper applying best evidence to surgical interventions [1]. It pulled together evidence about perioperative medicine, performed a systematic review of pilot studies, and suggested mechanisms of implementation. The surgical literature has many good meta-analyses. One, on techniques of vein harvesting for coronary artery bypass surgery [2], examines how different techniques can lead to very different rates of harmful postoperative leg wound infections.

Systematic review

The search used MEDLINE for studies reporting on minimally invasive vein harvesting for CABG, and compared it with conventional harvesting techniques. For inclusion studies had to be properly randomised, though clearly they could not be blind, and care was taken to avoid double-reporting. Minimally invasive methods included several techniques and instrumentation, including endoscopic techniques. Conventional vein harvesting used standard surgical instrumentation and direct visualisation through longitudinal or skin-bridging techniques to harvest the vein.

The outcome of postoperative leg wound infection was defined as drainage of pus from the wound, documented infection with positive culture, or the requirement for additional surgical or medical treatment, like use of antibiotics.

Results

There were 14 included trials with 1,527 patients. Trials were as large as 250 patients, and as small as 30. There were variable rates of conversion from minimally invasive to conventional harvesting, up to 22% in one trial. The follow up was variable, being as short as six days and as long as 42 days after the operation.

Leg wound infection rates varied between 3% and 30% (mean 13%) with conventional techniques, and 0% and 10% (mean 3%) with minimally invasive techniques (Figure 1). The number needed to treat with minimally invasive harvesting to prevent one leg wound infection that would have occurred with conventional harvesting was 10 (95% CI 8 to 14). The same result was found for larger and smaller trials (smaller trials had 65 patients or fewer), and for endoscopic harvesting (Table 1).

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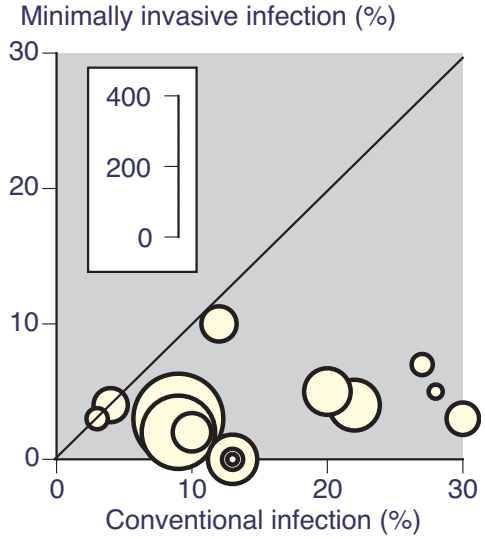
Figure 1: Infection rates for conventional and minimally invasive vein harvesting



Comment

Minimally invasive vein harvesting probably costs more and takes longer, but reduces postoperative leg wound infection significantly. Questions needing to be answered include whether it can be done in every institution, and whether it is cost-effective. Given that hospital acquired infection can cost an average of £3,150 and lead to an extra 14 days in hospital, as well as killing some patients, the answer looks obvious. More fun work for our health economists.

Reference:

1 H Kehlet, DW Wilmore. Multimodal strategies to improve surgical outcomes. American Journal of Surgery 2002 193: 630-641.

2 T Athanasiou et al. Leg wound infection after coronary artery bypass grafting: a meta-analysis comparing minimally invasive versus conventional vein harvesting. Ann Thorac Surg 2003 76: 2141-2146.

Table 1: NNTs and sensitivity analysis for leg wound infections, comparing minimally invasive with conventional harvesting

Included studies	Number of Trials	Number of Patients	Relative risk (95% CI)	NNT (95% CI)
All studies	14	1527	0.24 (0.16 to 0.36)	10 (8 to 14)
Larger studies	7	1088	0.26 (0.16 to 0.43)	10 (8 to 15)
Smaller studies	7	439	0.21 (0.10 to 0.44)	9 (6 to 19)
Endoscopic only	11	1156	0.24 (0.15 to 0.39)	10 (7 to 14)